## SEQUENCE LISTING

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<110> Houghton, Michael
<120> HCV FUSION PROTEINS WITH MODIFIED NS3 DOMAINS
<130> PP19545.003 (2300-19545)
<150> 60/394,510
<151> 2002-07-08
<150> 60/393,694
<151> 2002-07-02
<150> 09/721,479
<151> 2000-11-22
<150> 60/167,502
<151> 1999-11-24
<160> 8
<170> PatentIn version 3.2
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<212> PRT
<213> Artificial
<220>
<223> epitope recognized by a Tcell receptor
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Ala Glu Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly
                                   10
<210> 3
<211> 546
<212> DNA
<213> Artificial
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| <220><br><223>          | DNA s            | -          | ence       | of a              | ı rep      | orese      | entat      | ive        | nati              | .ve,       | unmo       | odifi      | .ed N      | IS3 pr            | otease |
|-------------------------|------------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|--------|
| <400>                   | 3                |            |            |                   |            |            |            |            |                   |            |            |            |            |                   |        |
| atg go<br>Met Al<br>1   |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 48     |
| tgc at<br>Cys Il        |                  |            | -          |                   |            |            |            | _          |                   |            |            |            |            |                   | 96     |
| gag gt<br>Glu Va        |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 144    |
| atc aa<br>Ile As        |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 192    |
| atc go<br>Ile Al<br>65  |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 240    |
| caa ga<br>Gln As        |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 288    |
| ccc to<br>Pro Cy        |                  | -          |            |                   | _          | -          |            |            | _                 | _          | _          |            |            |                   | 336    |
| gat gt                  | c att            | ccc        | gtg        | cgc               | cgg        | cgg        | ggt        | gat        | agc               | agg        | ggc        | agc        | ctg        | ctg               | 384    |
| Asp Va                  | al Ile<br>115    | Pro        | Val        | Arg               | Arg        | Arg<br>120 | Gly        | Asp        | Ser               | Arg        | Gly<br>125 | Ser        | Leu        | Leu               |        |
| teg ed<br>Ser Pr<br>13  | o Arg            |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 432    |
| ttg to<br>Leu Cy<br>145 | gc ccc<br>ys Pro | gcg<br>Ala | ggg<br>Gly | cac<br>His<br>150 | gcc<br>Ala | gtg<br>Val | ggc<br>Gly | ata<br>Ile | ttt<br>Phe<br>155 | agg<br>Arg | gcc<br>Ala | gcg<br>Ala | gtg<br>Val | tgc<br>Cys<br>160 | 480    |
| acc co                  |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 528    |
| gag ad<br>Glu Th        |                  |            |            |                   |            |            |            |            |                   |            |            |            |            |                   | 546    |

<210> 4

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<211> 182
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<212> PRT

<213> Artificial

<220>

<223> amino acid sequence of a representative native unmodified NS3 protease domain

<400>

Met Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Leu Leu Gly
1 5 10 15

Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
20 25 30

Glu Val Gln Ile Val Ser Thr Ala Ala Gln Thr Phe Leu Ala Thr Cys 35 40 45

Ile Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr 50 55 60

Ile Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp
65 70 75 80

Gln Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr 85 90 95

Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala 100 105 110

Asp Val Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu 115 120 125

Ser Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu 130 135 140

Leu Cys Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys 145 150 155 160

Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Asn Leu 165 170 175

Glu Thr Thr Met Arg Ser 180

<210> 5

<211> 5676

<212> DNA

<213> Artificial

<220>

<223> DNA sequence of a representative modified fusion protein, with the NS3 protease domain deleted from the N-terminus and including amino acids 1-121 of Core on the C-terminus

|   |   |   |   | gca<br>Ala<br>5   |   |   |   |   |   |   |   |   |   |   |   | 48  |
|---|---|---|---|-------------------|---|---|---|---|---|---|---|---|---|---|---|-----|
|   |   |   |   | aca<br>Thr        |   |   |   |   |   |   |   |   |   |   |   | 96  |
|   |   | - |   | aac<br>Asn        |   |   |   |   |   | _ |   |   |   |   |   | 144 |
| - |   |   | - | tac<br>Tyr        |   |   |   |   | _ |   |   | _ | _ |   |   | 192 |
| _ | _ |   |   | gct<br>Ala        |   | _ |   |   |   | _ | _ | _ | _ |   |   | 240 |
|   |   |   |   | tcc<br>Ser<br>85  |   |   |   |   |   |   |   |   |   |   |   | 288 |
|   |   |   |   | gcg<br>Ala        | _ | _ | - |   |   | - |   | _ |   |   | - | 336 |
|   |   |   |   | gtg<br>Val        |   |   |   |   |   | _ |   | _ | - | _ |   | 384 |
|   |   |   |   | atc<br>Ile        |   |   |   |   |   |   |   |   |   |   |   | 432 |
|   |   |   |   | aga<br>Arg        |   |   |   |   |   |   |   |   |   |   |   | 480 |
|   |   |   |   | gca<br>Ala<br>165 |   |   |   |   |   |   |   |   | - |   | _ | 528 |
|   |   |   |   | ctt<br>Leu        |   |   |   |   |   |   |   |   |   |   |   | 576 |
|   |   |   |   | acc<br>Thr        |   |   |   |   |   |   |   |   |   |   |   | 624 |
|   |   |   |   | gac<br>Asp        |   |   | _ | - | _ |   | _ |   | - | - |   | 672 |

| - |   | _   |   |   | acc<br>Thr            |   |   |   |   | _   |   |   |   | - | 720  |
|---|---|-----|---|---|-----------------------|---|---|---|---|-----|---|---|---|---|------|
| - | _ |     | _ |   | cgt<br>Arg            |   |   |   |   | -   |   |   |   |   | 768  |
|   |   |     | _ |   | <br>gca<br>Ala        | _ |   |   | _ |     |   |   | _ |   | 816  |
|   |   |     |   |   | gag<br>Glu            |   |   |   |   |     |   |   |   |   | 864  |
|   |   |     |   | _ | <br>act<br>Thr<br>295 |   | _ |   |   |     |   |   | _ |   | 912  |
|   | _ | 222 |   |   | <br>tgc<br>Cys        | _ | _ |   |   | _   |   |   |   |   | 960  |
| _ |   |     |   |   | cat<br>His            |   | _ | _ |   |     |   |   | _ |   | 1008 |
| _ |   | _   |   |   | ctt<br>Leu            |   |   | _ | _ |     |   |   | _ |   | 1056 |
|   | - | -   |   | - | gcc<br>Ala            |   |   |   |   |     | _ | - | _ |   | 1104 |
|   |   |     |   | _ | aag<br>Lys<br>375     |   |   |   |   | 555 |   |   |   | , | 1152 |
|   |   |     |   |   | gtt<br>Val            |   |   |   |   |     |   |   |   |   | 1200 |
| - |   |     |   |   | aca<br>Thr            | _ | _ | _ | _ | -   | _ |   | _ | _ | 1248 |
|   |   |     |   |   | gtt<br>Val            |   |   |   |   |     |   |   |   |   | 1296 |
|   |   |     |   |   | tgc<br>Cys            |   |   |   |   |     |   |   |   |   | 1344 |

|     | ggg<br>Gly<br>450 |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1392 |
|-----|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|     | gat<br>Asp        |     | -   | _   |     | -   |     |     |     |     | -   |     |     |     |     | 1440 |
|     | atg<br>Met        |     |     | -   |     | -   |     | -   | -   | _   | _   |     |     |     | _   | 1488 |
|     | acc<br>Thr        |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1536 |
|     | tgg<br>Trp        |     |     |     |     |     |     |     |     | _   |     | _   |     |     |     | 1584 |
|     | agt<br>Ser<br>530 |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1632 |
|     | gcc<br>Ala        |     | -   |     | _   | -   | -   |     |     | -   | -   | -   |     | -   |     | 1680 |
|     | acc<br>Thr        |     | _   |     |     |     |     |     |     |     | _   |     |     |     |     | 1728 |
| _   | gcc<br>Ala        | _   |     | _   | -   |     |     | _   | -   |     | -   |     |     |     | -   | 1776 |
|     | tta<br>Leu        |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1824 |
|     | gac<br>Asp<br>610 |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1872 |
|     | ttc<br>Phe        |     |     |     |     |     |     |     |     |     |     |     |     |     | -   | 1920 |
|     | cta<br>Leu        |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1968 |
|     | tgt<br>Cys        |     |     |     |     |     |     |     |     |     |     |     | -   | _   | -   | 2016 |
| gtg | cag               | tgg | atg | aac | cgg | ctg | ata | gcc | ttc | gcc | tcc | cgg | ggg | aac | cat | 2064 |

| Val | Gln               | Trp<br>675 | Met | Asn | Arg | Leu | Ile<br>680 | Ala | Phe | Ala | Ser | Arg<br>685 | Gly | Asn | His        |      |
|-----|-------------------|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|------------|------|
| -   | tcc<br>Ser<br>690 |            | _   |     |     |     | _          |     | -   | _   | _   | -          | -   | _   | -          | 2112 |
|     | gcc<br>Ala        |            |     | _   | _   |     |            | _   |     | -   |     | _          |     | -   | -          | 2160 |
|     | cag<br>Gln        |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2208 |
|     | agg<br>Arg        | _          |     |     | _   | -   |            | _   | _   |     |     | _          | _   |     | -          | 2256 |
|     | tgg<br>Trp        |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2304 |
|     | tcc<br>Ser<br>770 | _          |     |     |     |     |            |     |     |     | -   |            |     |     |            | 2352 |
| _   | cac<br>His        |            | _   | -   | _   | _   |            | _   |     |     |     |            |     | -   |            | 2400 |
|     | ggg<br>Gly        | _          | _   |     |     | -   |            |     |     |     | _   |            |     | _   |            | 2448 |
|     | Gly               |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2496 |
|     | cct<br>Pro        |            |     |     |     |     |            |     |     |     |     |            |     |     | gag<br>Glu | 2544 |
|     | tac<br>Tyr<br>850 |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2592 |
|     | act<br>Thr        |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2640 |
|     | ttc<br>Phe        |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2688 |
|     | aag<br>Lys        |            |     |     |     |     |            |     |     |     |     |            |     |     |            | 2736 |

| 900                 | 905                 | 910  |
|---------------------|---------------------|--|
|                     |                     | gag ccc gaa ccg gac gtg 2784<br>Glu Pro Glu Pro Asp Val<br>925       |
|                     | = =                 | tcc cat ata aca gca gag 2832<br>Ser His Ile Thr Ala Glu<br>940       |
|                     |                     | ccc ccc tct gtg gcc agc 2880<br>Pro Pro Ser Val Ala Ser<br>955 960   |
|                     | =                   | ctc aag gca act tgc acc 2928<br>Leu Lys Ala Thr Cys Thr<br>975       |
|                     |                     | ata gag gcc aac ctc cta 2976<br>Ile Glu Ala Asn Leu Leu<br>990       |
|                     |                     | agg gtt gag tca gaa aac 3024<br>Arg Val Glu Ser Glu Asn<br>1005      |
|                     |                     | ctt gtg gcg gag gag gac 3072<br>Leu Val Ala Glu Glu Asp<br>1020      |
| Glu Arg Glu Ile Ser | Val Pro Ala Glu Ile | ctg cgg aag tct cgg aga 3120<br>Leu Arg Lys Ser Arg Arg<br>1035 1040 |
|                     | Pro Val Trp Ala Arg | ccg gac tat aac ccc ccg 3168<br>Pro Asp Tyr Asn Pro Pro<br>1055      |
|                     |                     | gaa cca cct gtg gtc cat 3216<br>Glu Pro Pro Val Val His<br>1070      |
|                     | <del>-</del>        | cct gtg cct ccg cct cgg 3264<br>Pro Val Pro Pro Pro Arg<br>1085      |
|                     | <del>-</del>        | acc cta tct act gcc ttg 3312 Thr Leu Ser Thr Ala Leu 1100            |
|                     | Arg Ser Phe Gly Ser | tcc tca act tcc ggc att 3360<br>Ser Ser Thr Ser Gly Ile<br>1115 1120 |
|                     | Thr Thr Ser Ser Glu | ccc gcc cct tct ggc tgc 3408<br>Pro Ala Pro Ser Gly Cys<br>1135      |

| Pro Pro Asp Ser<br>1140  |   |  | tcc atg ccc ccc<br>Ser Met Pro Pro<br>1150  |   |
|--|---|--|---|---|
| ggg gag cct ggg<br>Gly Glu Pro Gly<br>1155   | Asp Pro Asp   |  |   |   |
| agt agt gag gcc<br>Ser Ser Glu Ala<br>1170   |   |  |   |   |
| tct tgg aca ggc<br>Ser Trp Thr Gly<br>1185   |   | Thr Pro Cys A  |   | -   |
| ctg ccc atc aat<br>Leu Pro Ile Asn   | -   |  | Leu Arg His His   | _   |
| gtg tat tcc acc<br>Val Tyr Ser Thr<br>1220   |   |  |   |   |
| aca ttt gac aga<br>Thr Phe Asp Arg<br>1235   | Leu Gln Val   |  |   | •   |
| aag gag gtt aaa<br>Lys Glu Val Lys<br>1250   |   |  |   |   |
| gta gag gaa gct  |   | acq ccc cca o  |   | 2040  |
| 1265   | 1270  | Thr Pro Pro I  | His Ser Ala Lys<br>275  | _   |
| 1265<br>ttt ggt tat ggg<br>Phe Gly Tyr Gly   | 1270<br>gca aaa gac   | Thr Pro Pro I  | His Ser Ala Lys<br>275<br>cat gcc aga aag<br>His Ala Arg Lys  | Ser Lys<br>1280<br>gcc gta 3888   |
| 1265<br>ttt ggt tat ggg<br>Phe Gly Tyr Gly   | 1270  gca aaa gac Ala Lys Asp 1285  tcc gtg tgg   | Thr Pro Pro I 12 gtc cgt tgc c Val Arg Cys I 1290 aaa gac ctt c  | His Ser Ala Lys<br>275<br>cat gcc aga aag<br>His Ala Arg Lys<br>ctg gaa gac aat   | Ser Lys<br>1280<br>gcc gta 3888<br>Ala Val<br>1295<br>gta aca 3936                                |
| ttt ggt tat ggg Phe Gly Tyr Gly acc cac atc aac Thr His Ile Asn  | gca aaa gac Ala Lys Asp 1285  tcc gtg tgg Ser Val Trp  acc atc atg Thr Ile Met              | Thr Pro Pro Pro Pro Pro Pro Pro Pro Pro Pr   | His Ser Ala Lys 275  cat gcc aga aag His Ala Arg Lys  ctg gaa gac aat Leu Glu Asp Asn 1310  gag gtt ttc tgc                                       | Ser Lys 1280  gcc gta 3888 Ala Val 1295  gta aca 3936 Val Thr  gtt cag 3984                       |
| ttt ggt tat ggg Phe Gly Tyr Gly  acc cac atc aac Thr His Ile Asn 1300  cca ata gac act Pro Ile Asp Thr | gca aaa gac Ala Lys Asp 1285  tcc gtg tgg Ser Val Trp  acc atc atg Thr Ile Met  ggt cgt aag | Thr Pro Pro II  gtc cgt tgc c Val Arg Cys II 1290  aaa gac ctt c Lys Asp Leu II 1305  gct aag aac c Ala Lys Asn c 320  cca gct cgt c | His Ser Ala Lys 275  cat gcc aga aag His Ala Arg Lys  ctg gaa gac aat Leu Glu Asp Asn 1310  gag gtt ttc tgc Glu Val Phe Cys 1325  ctc atc gtg ttc | Ser Lys 1280  gcc gta 3888 Ala Val 1295  gta aca 3936 Val Thr  gtt cag 3984 Val Gln  ccc gat 4032 |

| aag ctc ccc ttg gcc gtg atg gga agc tcc tac gga ttc caa tac tcc<br>Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser<br>1365 1370 1375      |        |
|---|--------|
| cca gga cag cgg gtt gaa ttc ctc gtg caa gcg tgg aag tcc aag aas<br>Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys<br>1380 1385 1390      |        |
| acc cca atg ggg ttc tcg tat gat acc cgc tgc ttt gac tcc aca gtc Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val 1395 1400 1405            |        |
| act gag agc gac atc cgt acg gag gag gca atc tac caa tgt tgt gad<br>Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys Cys Asp<br>1410 1415 1420      |        |
| ctc gac ccc caa gcc cgc gtg gcc atc aag tcc ctc acc gag agg ctt<br>Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu Arg Leu<br>1425 1430 1435 1440 | 1      |
| tat gtt ggg ggc cct ctt acc aat tca agg ggg gag aac tgc ggc tat<br>Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr<br>1445 1450 1455      |        |
| cgc agg tgc cgc gcg agc ggc gta ctg aca act agc tgt ggt aac acc<br>Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr<br>1460 1465 1470      |        |
| ctc act tgc tac atc aag gcc cgg gca gcc tgt cga gcc gca ggg ctc<br>Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala Gly Leu<br>1475 1480 1485      |        |
| cag gac tgc acc atg ctc gtg tgt ggc gac gac tta gtc gtt atc tgt<br>Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys<br>1490 1495 1500      |        |
| gaa agc gcg ggg gtc cag gag gac gcg gcg agc ctg aga gcc ttc acc<br>Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala Phe Thi<br>1505 1510 1515 1520 | c      |
| gag gct atg acc agg tac tcc gcc ccc cct ggg gac ccc cca caa cca<br>Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro<br>1525 1530 1535      |        |
| gaa tac gac ttg gag ctc ata aca tca tgc tcc tcc aac gtg tca gtc<br>Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val<br>1540 1545 1550      |        |
| gcc cac gac ggc gct gga aag agg gtc tac tac ctc acc cgt gac cct Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro 1555 1560 1565            |        |
| aca acc ccc ctc gcg aga gct gcg tgg gag aca gca aga cac act ccc Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro 1570 1580                 |        |
| gtc aat tcc tgg cta ggc aac ata atc atg ttt gcc ccc aca ctg tgc   | g 4800 |

| Val Asn<br>1585 | Ser Trp | Leu Gly<br>1590 | Asn Ile |         | Phe Ala<br>1595 | a Pro Thr                      | Leu Trp<br>1600 |      |
|-----------------|---------|-----------------|---------|---------|-----------------|--------------------------------|-----------------|------|
|                 | Met Ile |                 |         |         |                 | ctt ata<br>Leu Ile             |                 | 4848 |
|                 | _       |                 | Leu Asp |         |                 | ggg gcc<br>Gly Ala<br>1630     | _               | 4896 |
| Ser Ile         | _       | _               |         |         |                 | a aga ctc<br>n Arg Leu<br>1645 |                 | 4944 |
|                 |         | Ser Leu         |         |         |                 | gaa atc<br>Glu Ile             |                 | 4992 |
|                 |         |                 |         | Gly Val |                 | c ttg cga<br>D Leu Arg         |                 | 5040 |
|                 | Arg Ala |                 |         |         | Leu Lei         | g gcc aga<br>ı Ala Arg         |                 | 5088 |
|                 |         |                 | Lys Tyr |         |                 | g gca gta<br>p Ala Val<br>1710 |                 | 5136 |
| Lys Leu         |         |                 | -       |         |                 | g ctg gac<br>n Leu Asp<br>1725 | -               | 5184 |
|                 |         | Ala Gly         |         |         |                 | t tat cac<br>e Tyr His<br>)    |                 | 5232 |
|                 |         | _               |         | Trp Phe | -               | a ctc ctg<br>ı Leu Leu         | =               | 5280 |
|                 | Val Gly |                 |         |         | Arg Met         | g agc acg<br>t Ser Thr         |                 | 5328 |
|                 |         |                 | Lys Arg |         |                 | g cgg ccg<br>g Arg Pro<br>1790 |                 | 5376 |
| Val Lys         |         |                 |         |         |                 | a gtt tac<br>y Val Tyr<br>1805 |                 | 5424 |
|                 |         |                 |         |         |                 | g aga aag<br>r Arg Lys         |                 | 5472 |

| 1810  | 1815   | 1820   |  |
|---|--|--|--|
| gag cgg tcg caa cc<br>Glu Arg Ser Gln Pro<br>1825   |  |  |  |
| cgg ccc gag ggc ag<br>Arg Pro Glu Gly Arc<br>184  | g Thr Trp Ala  |  |  |
| tat ggc aat gag gg<br>Tyr Gly Asn Glu Gl<br>1860  | Cys Gly Trp  |  |  |
| ggc tct cgg cct ag<br>Gly Ser Arg Pro Se<br>1875  |  |  | Arg Ser Arg  |
| aat ttg ggt aag<br>Asn Leu Gly Lys<br>1890  |  |  | 5676   |
| <210> 6<br><211> 1892<br><212> PRT<br><213> Artificial  |  |  |  |
|   |  |  |  |
| with the NS   | 3 protease dom   | representative modi<br>ain deleted from th<br>21 of Core on the C  |  |
| <223> amino acid with the NS  | 3 protease dom   | ain deleted from th  | ne N-terminus and  |
| <223> amino acid with the NS including as <400> 6  Met Ala Ala Tyr Al   | 3 protease dom<br>mino acids 1-1   | ain deleted from th<br>21 of Core on the (   | ne N-terminus and<br>C-terminus  |
| <223> amino acid with the NS including as <400> 6  Met Ala Ala Tyr Al   | 3 protease dom<br>mino acids 1-1<br>a Ala Gln Gly<br>5<br>r Leu Gly Phe  | ain deleted from th<br>21 of Core on the C<br>Tyr Lys Val Leu Val<br>10  | ne N-terminus and<br>C-terminus<br>Leu Asn Pro<br>15   |
| <223> amino acid with the NS including at <400> 6  Met Ala Ala Tyr Al 1  Ser Val Ala Ala Th   | 3 protease dom<br>mino acids 1-1<br>a Ala Gln Gly<br>5<br>r Leu Gly Phe  | ain deleted from the C<br>21 of Core on the C<br>Tyr Lys Val Leu Val<br>10<br>Gly Ala Tyr Met Sen<br>25  | Leu Asn Pro 15 Lys Ala His 30  |
| <223> amino acid with the NS including at 4400> 6  Met Ala Ala Tyr Al 1  Ser Val Ala Ala Th 20  Gly Ile Asp Pro As  | 3 protease dom<br>mino acids 1-1<br>a Ala Gln Gly<br>5<br>r Leu Gly Phe<br>n Ile Arg Thr<br>40                                   | ain deleted from the C<br>21 of Core on the C<br>Tyr Lys Val Leu Val<br>10<br>Gly Ala Tyr Met Sen<br>25<br>Gly Val Arg Thr Ile                                     | Leu Asn Pro 15 Lys Ala His 30 Thr Thr Gly  |
| <223> amino acid with the NS including at 4400> 6  Met Ala Ala Tyr Al 1  Ser Val Ala Ala Th 20  Gly Ile Asp Pro As 35  Ser Pro Ile Thr Ty   | 3 protease dom mino acids 1-1  a Ala Gln Gly b Leu Gly Phe n Ile Arg Thr 40 r Ser Thr Tyr 55                                     | ain deleted from the C21 of Core on the C3  Tyr Lys Val Leu Val 10  Gly Ala Tyr Met Sen 25  Gly Val Arg Thr Ile 45  Gly Lys Phe Leu Ala 60                         | ne N-terminus and C-terminus  Leu Asn Pro 15  Lys Ala His 30  Thr Thr Gly  A Asp Gly Gly               |
| <pre>&lt;223&gt; amino acid     with the NS     including at &lt;400&gt; 6  Met Ala Ala Tyr Al     1  Ser Val Ala Ala Th     20  Gly Ile Asp Pro As     35  Ser Pro Ile Thr Ty     50  Cys Ser Gly Gly Al</pre> | B protease dommino acids 1-1  A Ala Gln Gly  T Leu Gly Phe  A Ile Arg Thr  40  T Ser Thr Tyr  55  Tyr Asp Ile  70  T Ile Leu Gly | ain deleted from the C21 of Core on the C3  Tyr Lys Val Leu Val 10  Gly Ala Tyr Met Sen 25  Gly Val Arg Thr Ile 49  Gly Lys Phe Leu Ala 60  Ile Ile Cys Asp Glu 75 | ne N-terminus and C-terminus  Leu Asn Pro 15  Lys Ala His 30  Thr Thr Gly  Asp Gly Gly  Cys His Ser 80 |

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser

115 120 125 Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val 135 Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val 185 Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe 215 220 Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile Thr Leu Pro Gln Asp 225 230 Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg Pro Ser Gly Met Phe 260 270 265 Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Gly 315 305 310

Val Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr 325 330 335

Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val Ala Tyr Gln Ala Thr 340 345 350

Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp 355 360 365

Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu 370 375 380

Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile Thr Leu Thr His Pro 385 390 395 400

Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala Asp Leu Glu Val Val
405 410 415

Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala

420 425 430

Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val Val Leu 440 Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln 470 475 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu 490 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe 520 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn 530 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val 565 570 575 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val 610 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val 630 635 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val 645 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val 695 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu 710 715 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp

| 725 | 730 | 735 |
|-----|-----|-----|
|     |     |     |

- Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys 740 745 750
- Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
  755 760 765
- Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile 770 780
- Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys 785 790 795 800
- Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp 805 810 815
- Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro 820 825 830
- Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser Ala Glu 835 840 845
- Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly 850 855 860
- Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu 865 870 875 880
- Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro 885 890 895
- Cys Lys Pro Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His  $900 \hspace{1.5cm} 905 \hspace{1.5cm} 910$
- Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val 915 920 925
- Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu 930 935 940
- Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser 945 950 955 960
- Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr 965 970 975
- Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu 980 985 990
- Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn 995 1000 1005
- Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp 1010 1015 1020
- Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Arg Arg

|      | 1000 | 1005 | 1010 |
|------|------|------|------|
| 1025 | 1030 | 1035 | 1040 |

- Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro Asp Tyr Asn Pro Pro 1045 1050 1055
- Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val Val His
  1060 1065 1070
- Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Pro Arg 1075 1080 1085
- Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr Leu Ser Thr Ala Leu 1090 1095 1100
- Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser Gly Ile 1105 1110 1115 1120
- Thr Gly Asp Asn Thr Thr Ser Ser Glu Pro Ala Pro Ser Gly Cys 1125 1130 1135
- Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu 1140 1145 1150
- Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val 1155 1160 1165
- Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys Cys Ser Met Ser Tyr 1170 1175 1180
- Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys 1185 1190 1195 1200
- Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu 1205 1210 1215
- Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys Lys Val 1220 1225 1230
- Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu 1235 1240 1245
- Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu Leu Ser 1250 1260
- Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys 1265 1270 1275 1280
- Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys Ala Val 1285 1290 1295
- Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn Val Thr
  1300 1305 1310
- Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln 1315 1320 1325
- Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp

1335

1330

Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Thr 1345 1350 1355 1360

1340

- Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser 1365 1370 1375
- Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys 1380 1385 1390
- Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val 1395 1400 1405
- Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys Cys Asp 1410 1420
- Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu Arg Leu 1425 1430 1435 1440
- Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr 1445 1450 1455
- Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr 1460 1465 1470
- Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala Gly Leu 1475 1480 1485
- Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys 1490 1495 1500
- Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala Phe Thr 1505 1510 1515 1520
- Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro  $1525 \hspace{1cm} 1530 \hspace{1cm} 1535$
- Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val 1540 1545 1550
- Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro 1555 1560 1565
- Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro 1570 1580
- Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp 1585 1590 1595 1600
- Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg 1605 1610 1615
- Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr 1620 1630
- Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly

1635 1640 1645

Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg 1650 1660

Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Ala Trp 1665 1670 1675 1680

Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg Gly Gly
1685 1690 1695

Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Arg Thr 1700 1705 1710

Lys Leu Lys Leu Thr Pro Ile Ala Ala Gly Gln Leu Asp Leu Ser 1715 1720 1725

Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Val 1730 1740

Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys Leu Leu Leu Leu Ala 1745 1750 1755 1760

Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg Met Ser Thr Asn Pro 1765 1770 1775

Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn Arg Arg Pro Gln Asp 1780 1785 1790

Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly Gly Val Tyr Leu Leu 1795 1800 1805

Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala Thr Arg Lys Thr Ser 1810 1815 1820

Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro Ile Pro Lys Ala Arg 1825 1830 1835 1840

Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly Tyr Pro Trp Pro Leu 1845 1850 1855

Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp Leu Leu Ser Pro Arg 1860 1865 1870

Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro Arg Arg Arg Ser Arg 1875 1880 1885

Asn Leu Gly Lys 1890

<210> 7

<211> 21

<212> PRT

<213> Artificial

<220>

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<223> E2 epitope consensus sequence
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                                  10
Gly Ala Lys Gln Asn
           20
<210> 8
<211> 23
<212> PRT
<213> Artificial
<220>
<223> NS4A peptide
<400> 8
Lys Lys Gly Ser Val Val Ile Val Gly Arg Ile Val Leu Ser Gly Lys
                                  10
Pro Ala Ile Ile Pro Lys Lys
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20